CytomX Therapeutics

PROCLAIM CX-072

SITC 2018 Clinical Presentation

November 10, 2018

Forward Looking Statements

Special Note Regarding Forward-Looking Statements

This presentation may contain projections and other forward-looking statements regarding future events. All statements other than statements of historical facts contained in this presentation, including statements regarding our future financial condition, technology platform, development strategy, prospective products, preclinical and clinical pipeline and milestones, regulatory objectives, expected payments from and outcomes of collaborations, and likelihood of success, are forward-looking statements. Such statements are predictions only and involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. These risks and uncertainties include, among others, the costs, timing and results of preclinical studies and clinical trials and other development activities; the uncertainties inherent in the initiation and enrollment of clinical trials; expectations of expanding on-going clinical trials; availability and timing of data from clinical trials; the unpredictability of the duration and results of regulatory review; market acceptance for approved products and innovative therapeutic treatments; competition; the potential not to receive partnership milestone, profit sharing or royalty payments; the possible impairment of, inability to obtain and costs of obtaining intellectual property rights; and possible safety or efficacy concerns, general business, financial and accounting risks and litigation. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. More information concerning us and such risks and uncertainties is available on our website and in our press releases and in our public filings with the U.S. Securities and Exchange Commission. We are providing this information as of its date and do not undertake any obligation to update or revise it, whether as a result of new information, future events or circumstances or otherwise. Additional information may be available in press releases or other public announcements and public filings made after the date of this presentation.

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CytomX Therapeutics

Introduction

Sean McCarthy, D. Phil.
President and Chief Executive Officer

Reinventing Therapeutic Antibodies

- Antibodies are a very successful therapeutic class in many disease areas
  - 2017: Half of the top 10 selling drugs were mAbs
- Major opportunity to target antibodies to disease tissue
  - Enable new targets/mechanisms
  - Reduce toxicities
  - Maximize efficacy
- CytomX is targeting cancer tissue using Probody™ Therapeutics
  - A versatile platform
  - Leverages intrinsic protease activity in tumors

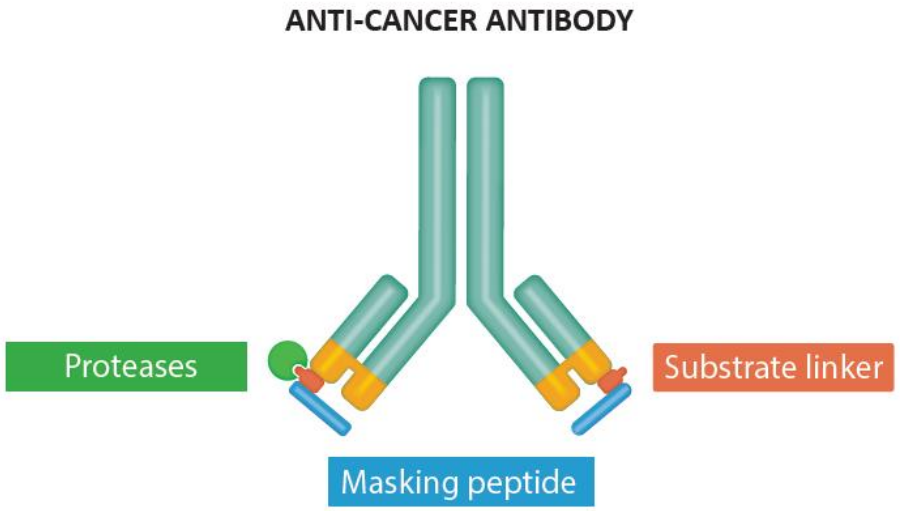
Proteases: Active in Tumor Tissue

Imaging of Active Protease[1]

1. Matriptase: LeBeau, et al., PNAS 2012

Probody Therapeutics: Activated in Tumor Tissue

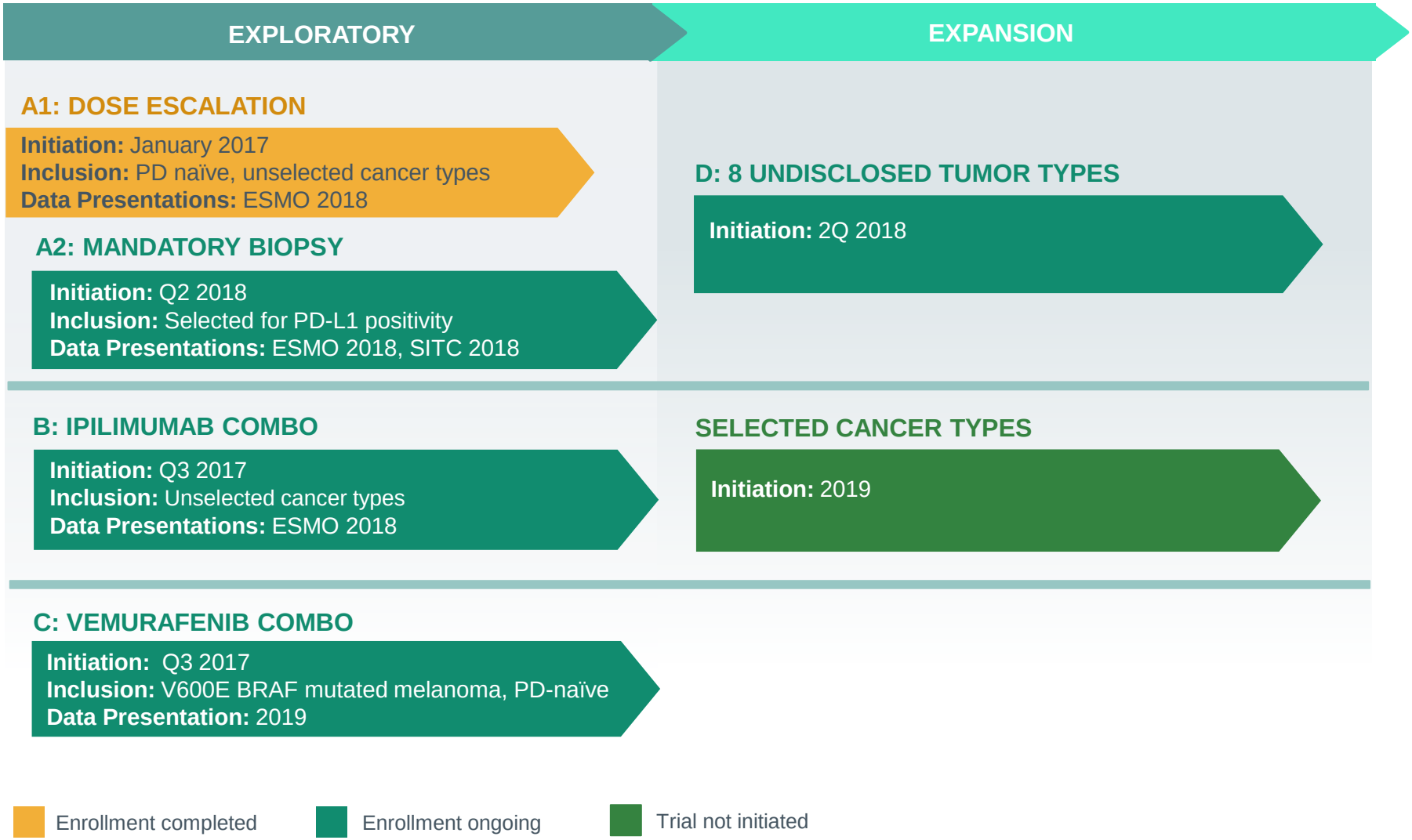
CytomX Data Presented in 2018 Provides Early Validation for Clinical Performance of the Probody Platform



Key Elements of the Probody Platform

- Stability in Periphery
- Improved Safety
- Activation in Tumor
- Anti-Cancer Activity

PROCLAIM-CX-072 Clinical Trial Design



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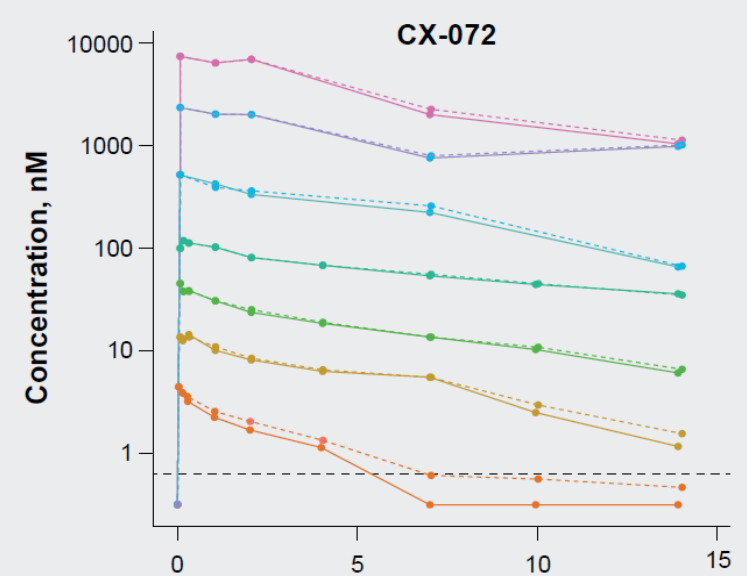
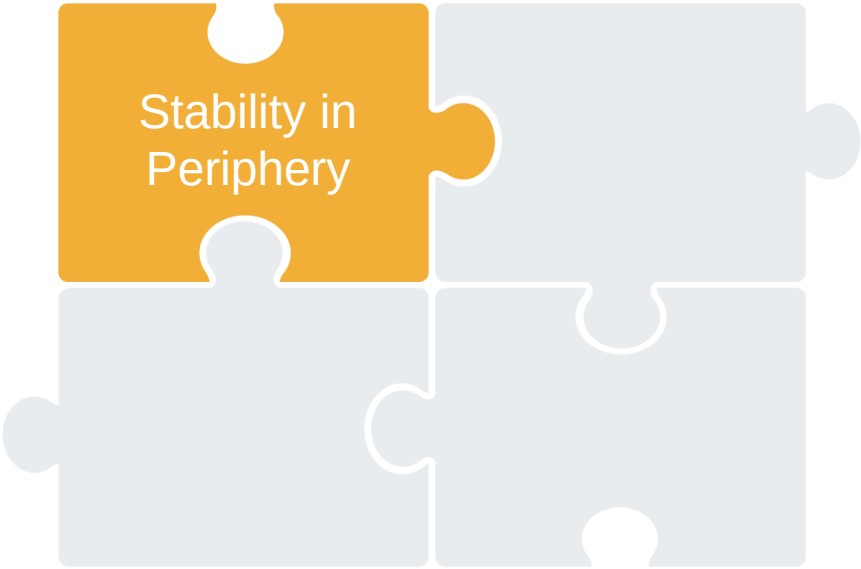
Clinical PK Shows Probody Therapeutics Can Remain Effectively Masked in Systemic Circulation

PROCLAIM-CX-072 Clinical Studies

ASCO ESMO

Predominant species in circulation is masked and intact Probody





- Total (dashed lines) and intact/masked CX-072 (solid lines) concentrations are highly similar following first dose over two weeks from 0.03 mg/kg to 30 mg/kg
- For example, at 10 mg/kg, 95% of the circulating CX-072 is intact/masked

Probody Therapeutics Can Widen the Safety Window

PROCLAIM-CX-072 Clinical Studies

ASCO ESMO

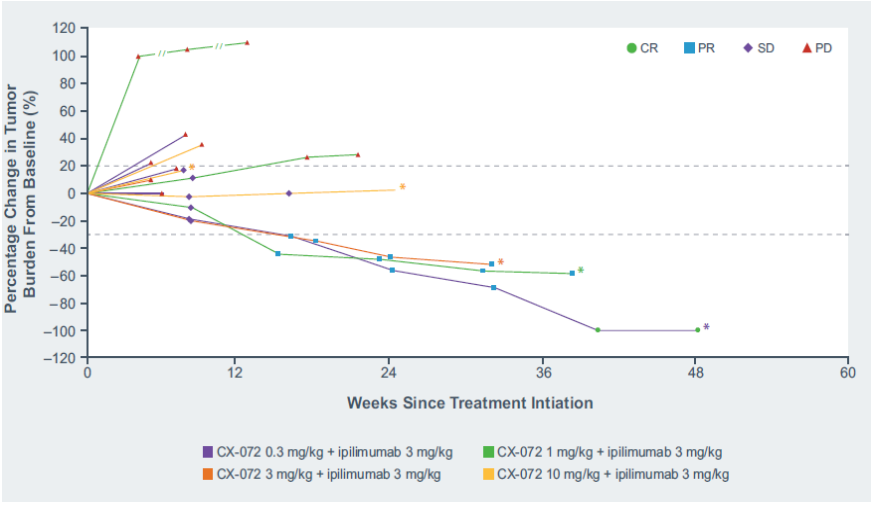
- *Favorable Safety Profile as Monotherapy*
  - 11% Grade 3/4 TRAE
  - 7% irAE
- *Potentially Differentiated Safety Profile in Ipilimumab (3 mg/kg) Combination*
  - 20% Grade 3/4 treatment related adverse events trending below historical[1]
  - 10% irAE

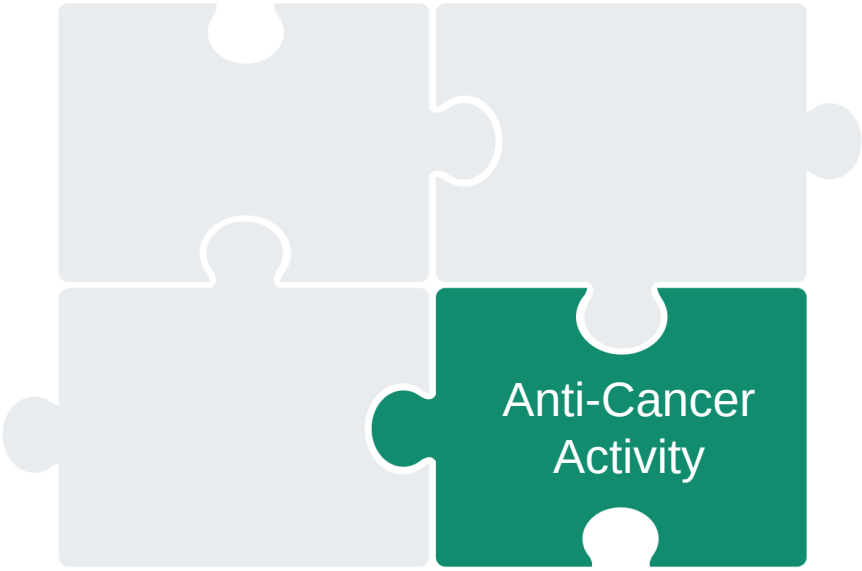
1. Larkin et al., NEJM, July 2015.

Probody Therapeutics Demonstrate Durable Anti-Cancer Activity Across a Range of Tumor Types

PROCLAIM-CX-072 Clinical Studies

- *Monotherapy*
  - 3 (17%) treated at ≥ 3 mg/kg objective responses: 1 confirmed response and 2 unconfirmed partial responses
- *Yervoy® combo*
  - 3 (21%) confirmed objective responses, including 1 confirmed complete response





Validation of Probody Therapeutic Activation within the Tumor Microenvironment

Preliminary analysis of on-treatment tumor biopsies for biomarkers and CX-072 Probody activation within the tumor

CX-072 Clinical Data Presentations
2018 SITC Annual Meeting

Poster #P87

Preliminary Evidence of Intratumoral Activation and Immunomodulatory Effect of CX-072, a Probody Therapeutic Antibody Prodrug Targeting PD-L1, in a Phase 1/2a Trial

- Presenter: Luc Desnoyers, Ph.D., Senior Director of Translational Sciences, CytomX Therapeutics
- Date/Time: November 9, 2018; 8:00 – 9:00 a.m. / 12:45 – 2:15 p.m. / 6:30 - 8:30 p.m. EST
- Location: Poster Hall E, Walter E. Washington Convention Center

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Rapid Fire Oral Session

Preliminary Evidence of Intratumoral Activation and Immunomodulatory Effect of CX-072, a Probody Therapeutic Antibody Prodrug Targeting PD-L1, in a Phase 1/2a Trial

- Presenter: Luc Desnoyers, Ph.D., Senior Director of Translational Sciences, CytomX Therapeutics
- Date/Time: November 10, 2018; 1:05 - 1:10 p.m. EST
- Location: Poster Hall E, Walter E. Washington Convention Center

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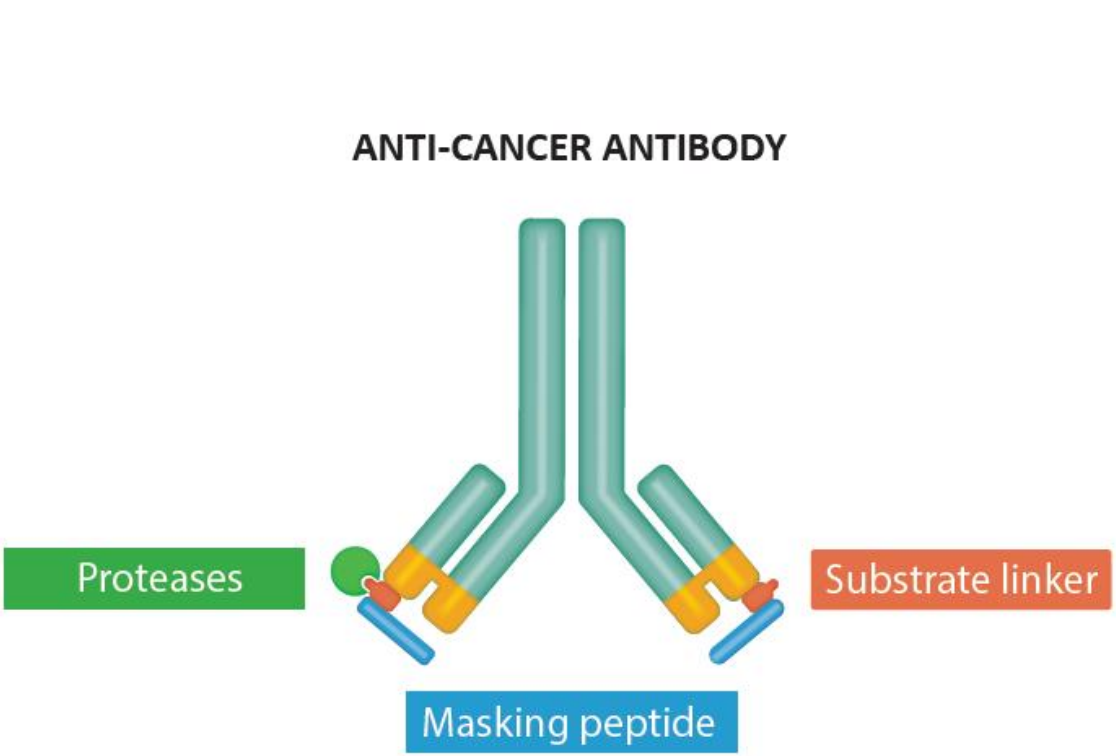
CytomX Therapeutics

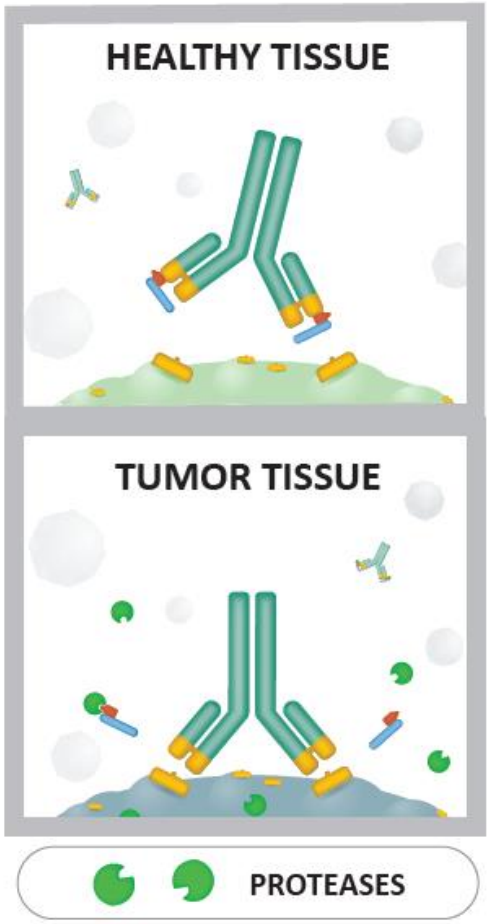
PROCLAIM-CX072 Preliminary Translational Results

W. Michael Kavanaugh, M.D.

Chief Scientific Officer and Head of Research and Non-Clinical Development

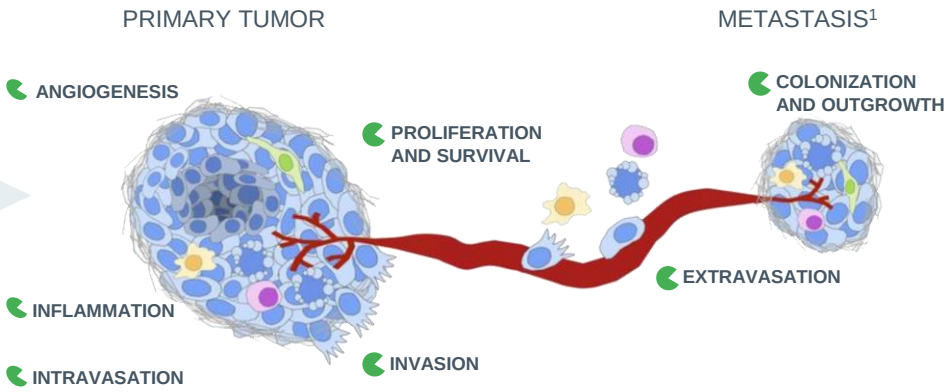
Probody Therapeutics:
Protease-Activatable Antibody Prodrugs



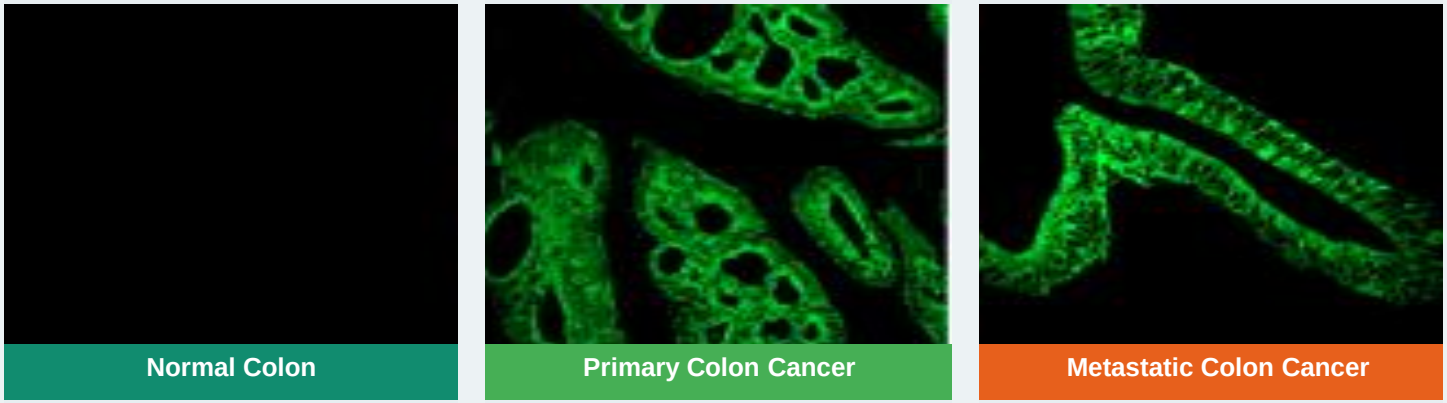


Activated Extracellular Proteases are Prevalent in Tumors But Not in Healthy Tissue

- Upregulated protease activity is a hallmark of all cancers
- Protease activity is tightly controlled in healthy tissues



IMAGING OF ACTIVE PROTEASE[2]



1. Sevenich, et. Al. Gene & Dev., 2014; 2. Matriptase: LeBeau, et al., PNAS 2012

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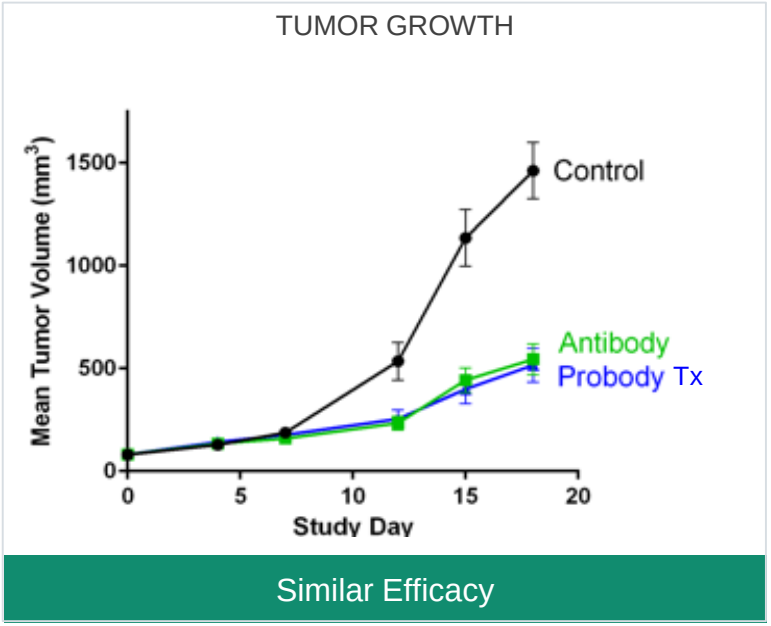
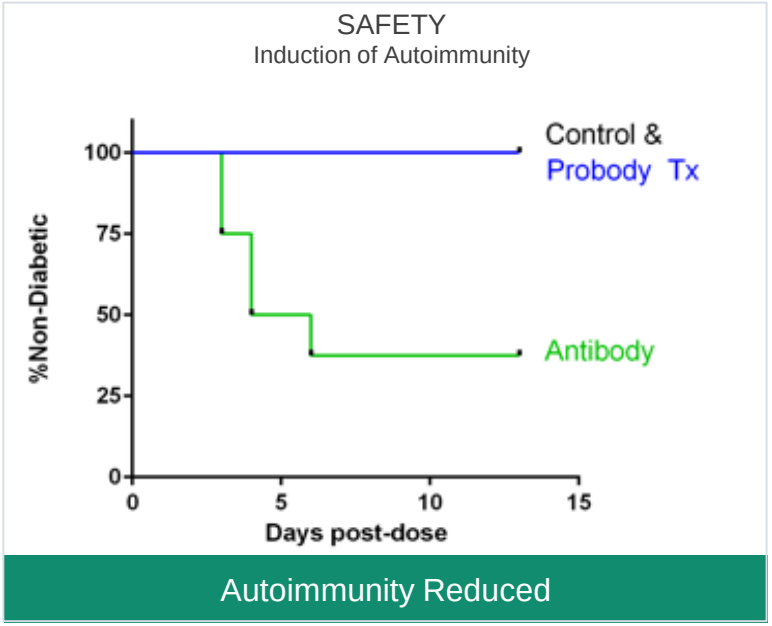
Preclinical Proof of Concept for CX-072:
A PD-L1 Probody Therapeutic with Antitumor Efficacy, Improved Safety

TUMOR GROWTH



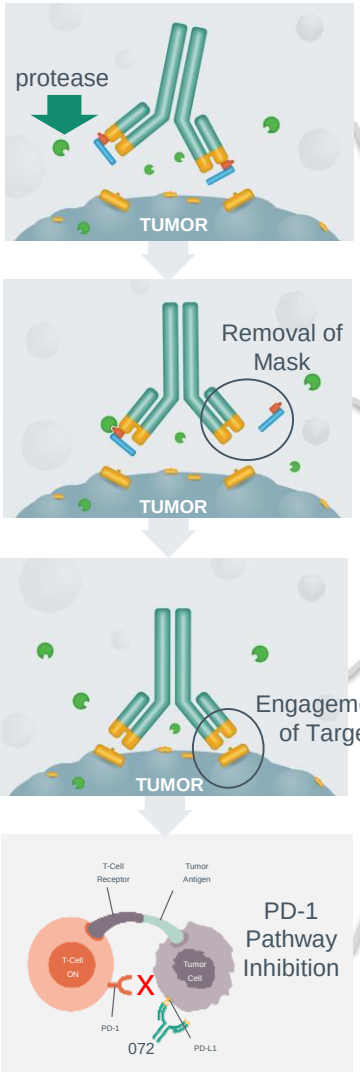
Similar Efficacy

SAFETY
Induction of Autoimmunity



Autoimmunity Reduced

CX-072 Translational Program is Designed to Provide Evidence of Probody MOA and Biological Activity in Patients



Potential Predictive Markers	• PD-L1 levels in tumor (IHC)* • Relevant protease activity in patient biopsies • Tumor mutational burden*
Probody-Tx Activation in Tumor	• Probody-Tx activation/unmasking: analyzed by • capillary electrophoresis immunoassay
Probody-Tx Localization in Tumor	• ^{89}Zr-PET imaging*
PD-L1 / PD-1 Pathway Inhibition	• Markers of immune system activation: assessed by IHC and mRNA expression

*data not presented in the SITC 2018 poster

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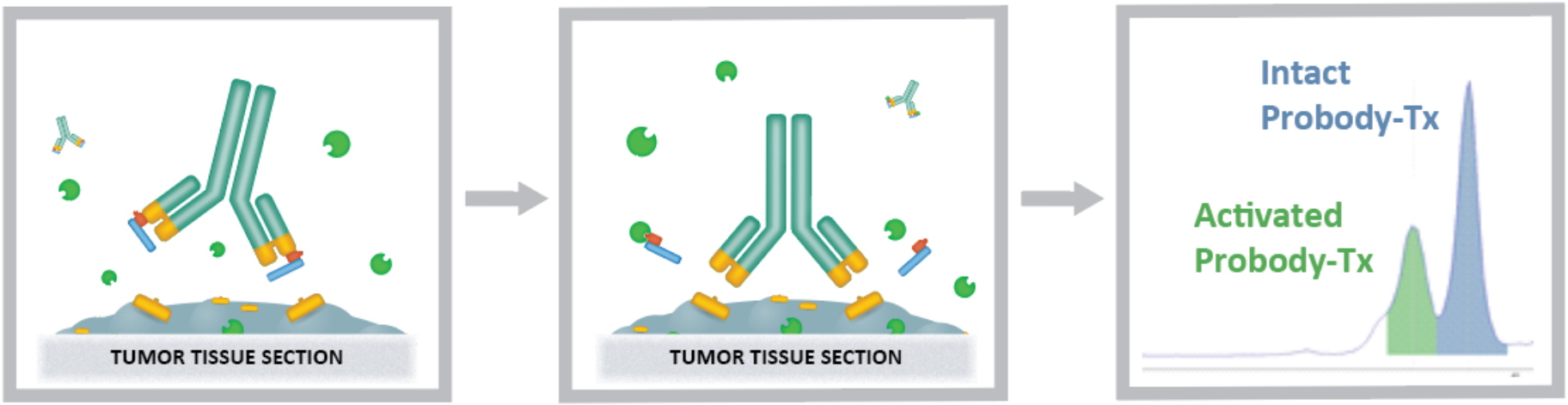
A Novel Method for Determining the Presence of Protease Activity in Pretreatment Biopsies

Incubate labeled Probody molecule with frozen tumor slices

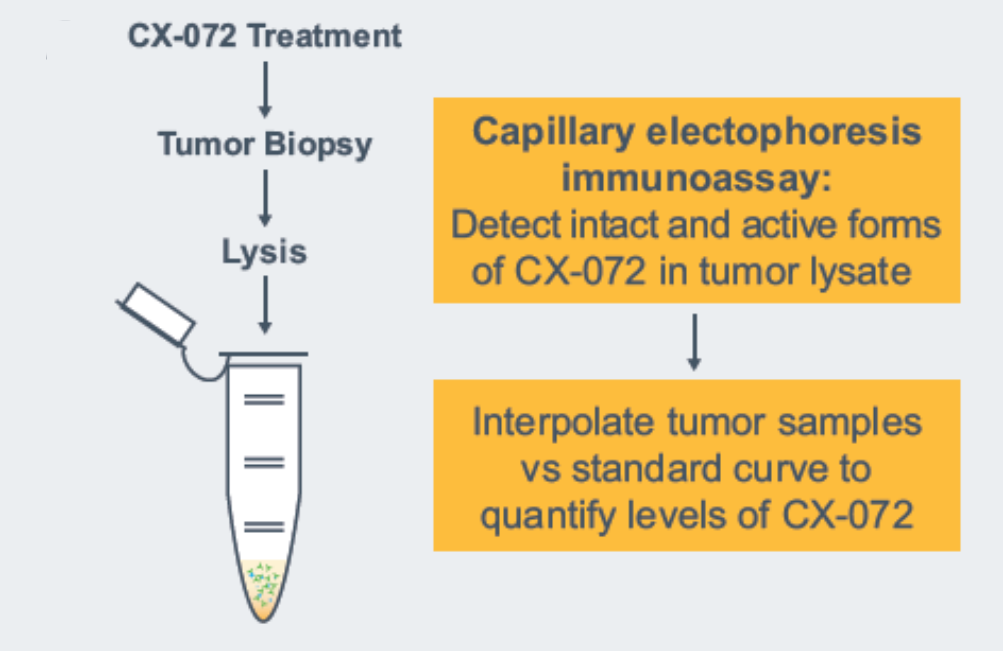
Proteases in tumor slice remove mask

Analyze Probody for unmasking by CE



- 15 of 18 (83%) evaluable PROCLAIM-CX-072 biopsies were categorized as positive for detectable protease activity in this assay
- Result consistent with protease detected in ~90% of commercial tumor samples

Probody Therapeutic Activation/Unmasking Measurement in Tumor Samples from CX-072–Treated Patients



- On-treatment biopsies were obtained from a subset of patients either 3-5 days after dose 1 or after 4-6 weeks of CX-072 therapy

Activated/Unmasked CX-072 Is Detected in Human Tumors at Doses ≥1 mg/kg

CX-072 Dose, mg/kg	Total CX-072, nM	Activated CX-072, nM
30	734.0	221.0
10	206.7	104.7
10	165.3	65.4
10	120.8	31.0
10	57.7	10.2
10	72.5	6.6
3	55.6	8.5
3	13.0	3.8
3	28.2	3.8
3	13.3	Not detectable
3	2.6	Not detectable
3	1.1	Not detectable
3	Below LLOQ	Not detectable
3	Below LLOQ	Not detectable
1	18.8	6.4
1	6.5	Not detectable
1	Not detectable	Not detectable
1	Not detectable	Not detectable
0.3	8.7	Not detectable
0.3	0.7	Not detectable
0.3	0.5	Not detectable
0.3	Below LLOQ	Below LLOQ
0.3	Not detectable	Not detectable

- Intratumoral total and activated CX-072 increased with dose
- First generation assay not sensitive enough to detect CX-072 in all tumors ≤ 3 mg/kg
- 10 mg/kg is being studied in Part D expansion cohorts

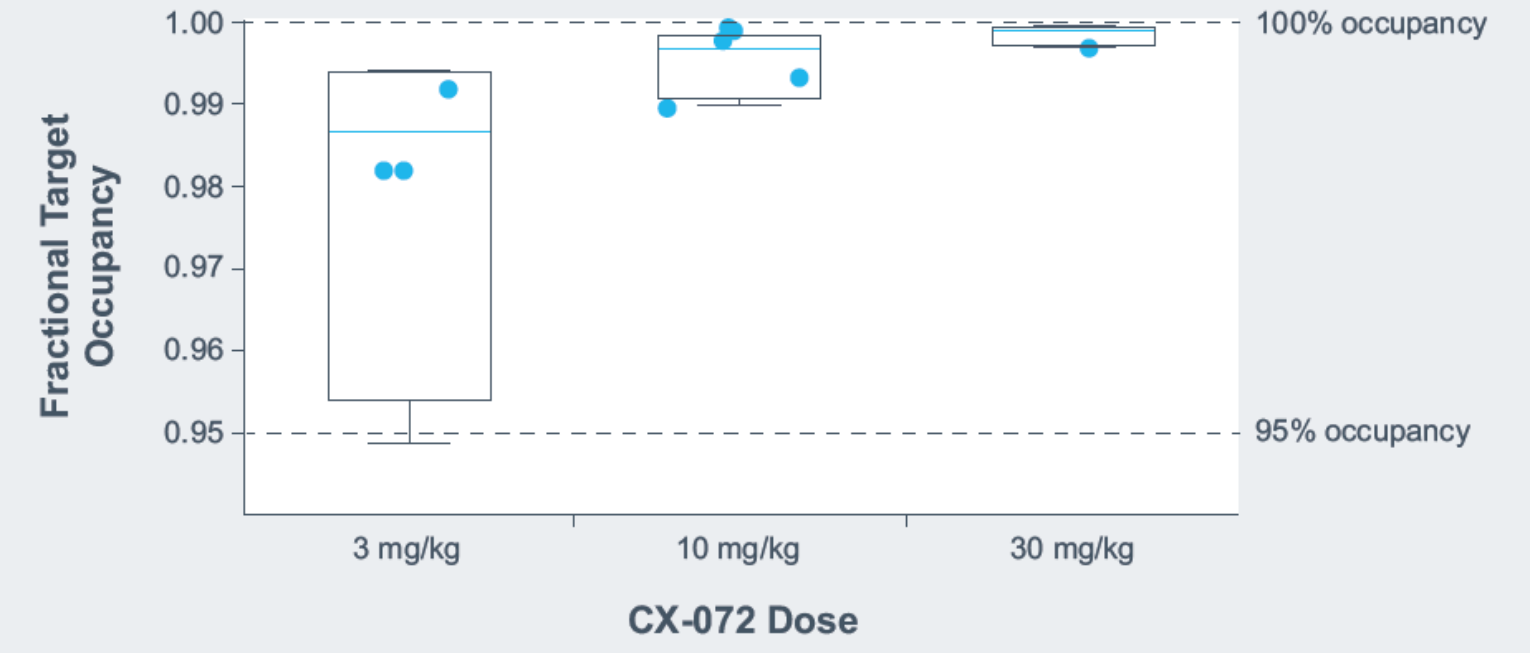
Estimated Intratumoral Target Occupancy of PD-L1 by Activated/Unmasked CX-072 Exceeds 98% at Doses ≥3 mg/kg

CX-072 Dose, mg/kg	Molar Ratio Activated CX-072: Median Reference PD-L1	Estimated Target Occupancy, %
30 (n = 1)	271	99.97
10 (n = 5)	116	99.65
3 (n = 3[a])	9	98.87

- For doses ≥10 mg/kg, the intratumoral concentration of unmasked/activated CX-072 was estimated to be ≥10x molar excess vs median PD-L1 concentration derived from a reference tumor set

PD-L1, programmed cell death ligand 1.
[a] For 3-mg/kg biopsy samples, table shows data only from 3 of 8 biopsies for which activated/unmasked CX-072 was detectable.

Estimated Intratumoral CX-072 Target Occupancy Is Similar To Predicted Values From A QSP* Model



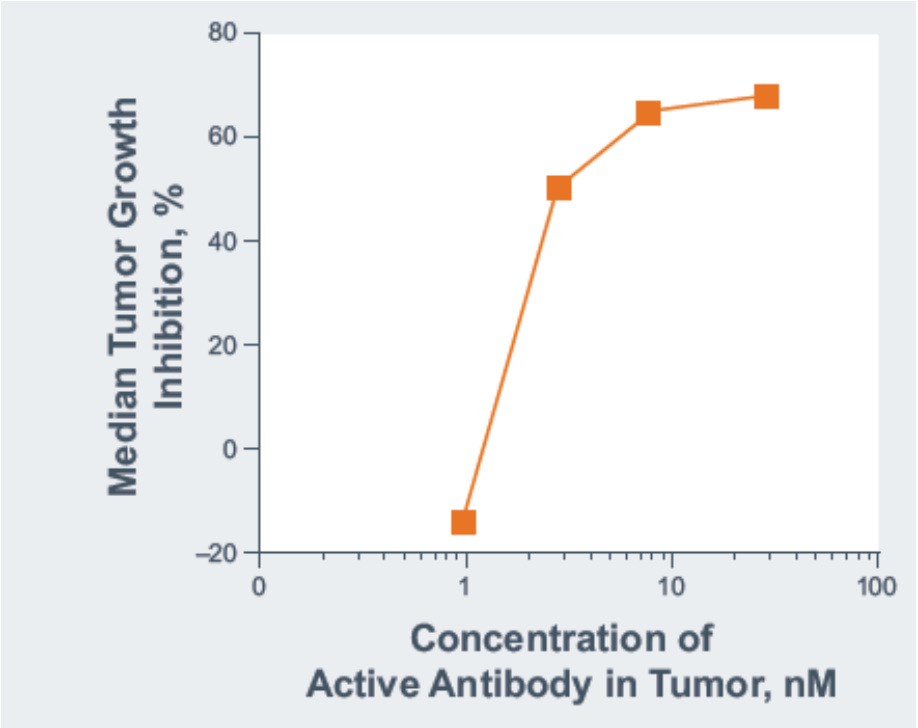
Blue dots: Estimated values for clinical biopsies

Box plots: Predicted values from models

Stroh M et al. *Clin Pharmacol Ther.* 2018;103(suppl):S88.

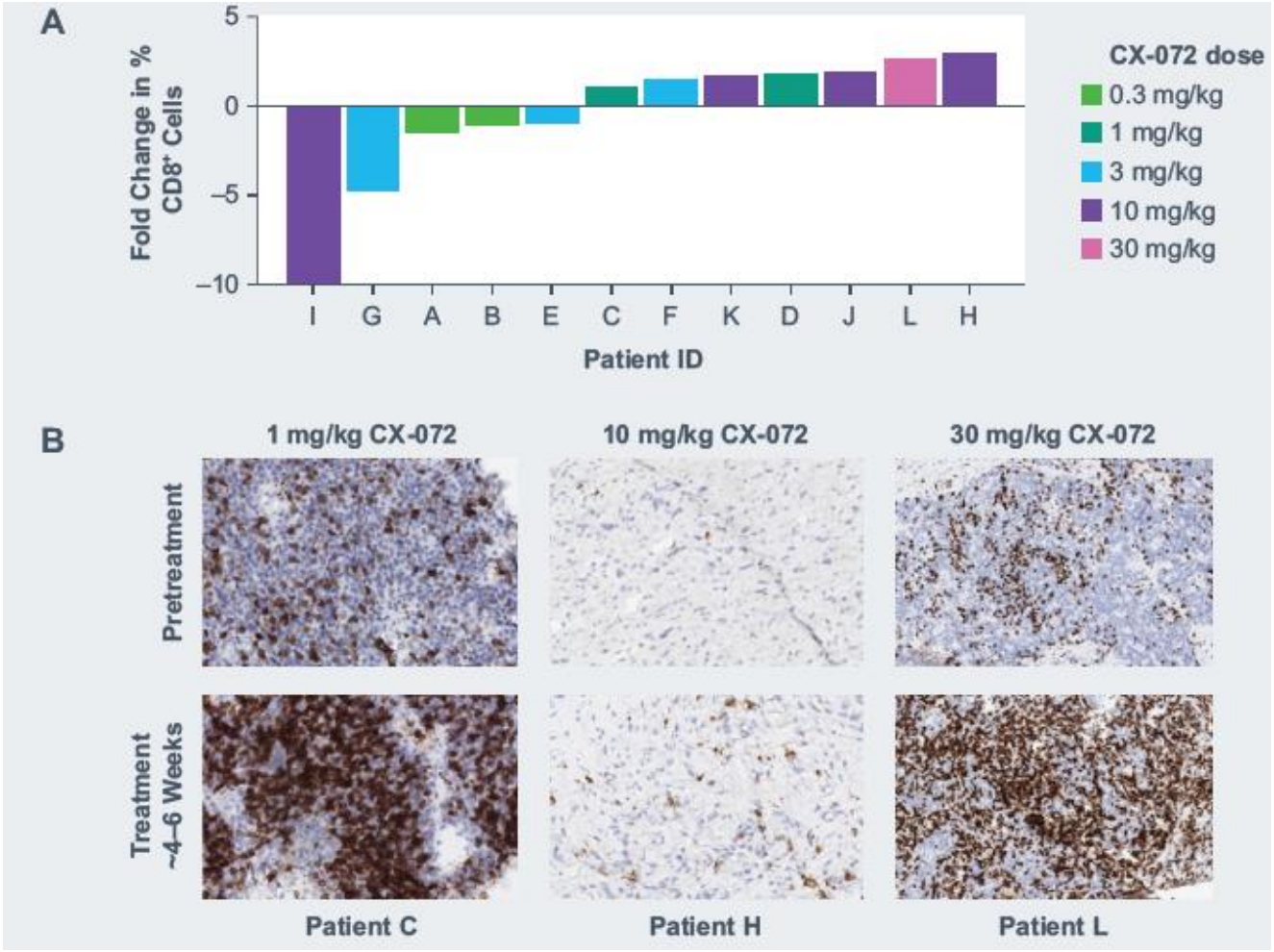
* *Quantitative Systems Pharmacology*

Active CX-072 Concentrations Achieved in Human Tumors Are Similar to Efficacious Concentrations in a Preclinical Model



Efficacious Intratumoral Concentrations in Preclinical Model	Achieved Intratumoral Concentrations in CX-072 Treated Patients (≥10 mg/kg)
2.8 - 126.5 nM (median 21 nM)	6.6 - 221 nM (median 48.2 nM)

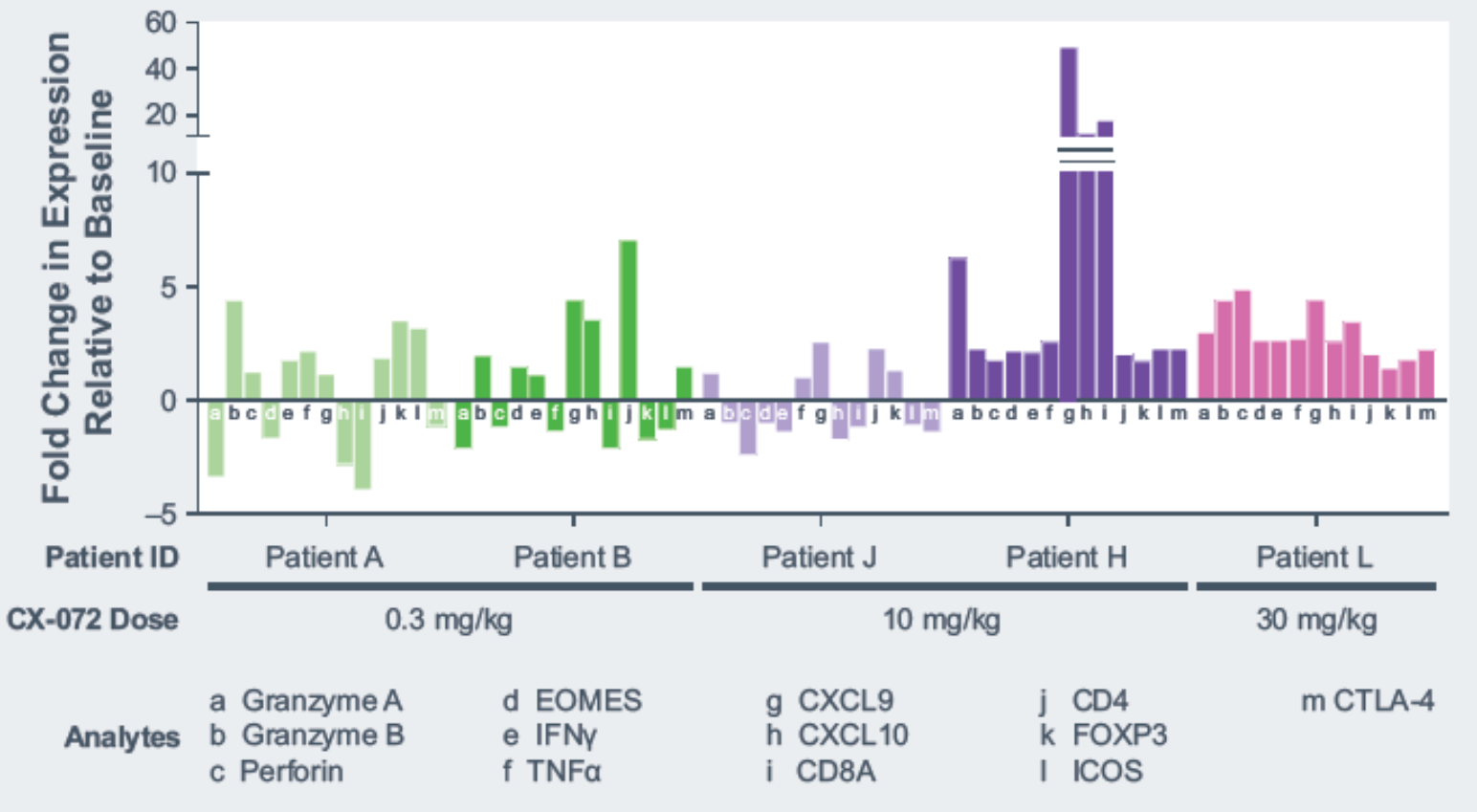
CX-072 Treatment Increases Levels of CD8+ T Cells in Patient Tumors



Consistent with inhibition of the PD-1: PD-L1 pathway

CytomX THERAPEUTICS

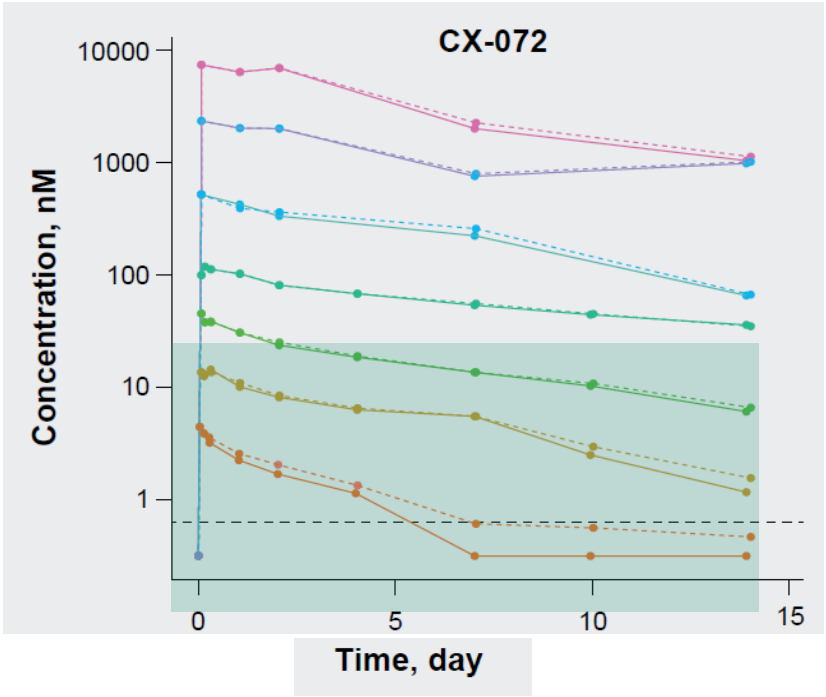
CX-072 Treatment Increases mRNA Expression of Markers of T-cell Activation in Patient Tumors

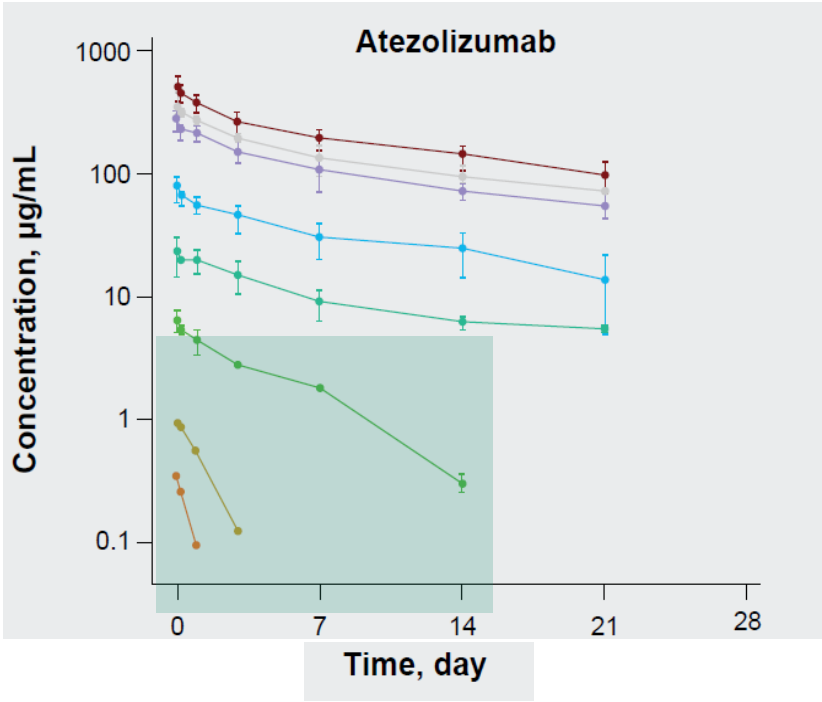


CTLA4, cytotoxic T-lymphocyte–associated protein 4; EOMES, eomesodermin; IFNγ, interferon gamma; TNFα, tumor necrosis factor α.

Consistent with inhibition of the PD-1: PD-L1 pathway

PROCLAIM-CX-072 Dose Escalation: Minimal Peripheral Target Engagement for CX-072





Published with permission Stroh et al. 2016. Clin Pharm Therap.

0.03 mg/kg | 0.1 mg/kg | 0.3 mg/kg | 1 mg/kg | 3 mg/kg | 10 mg/kg | 15 mg/kg | 20 mg/kg | 30 mg/kg

- Single-dose CX-072 PK data suggests that CX-072 circulates predominantly as the intact prodrug species
- Clearance is minimally influenced by target mediated drug disposition

PROCLAIM-CX-072 Clinical Translation: Summary

Proteolytic Activation of CX-072

- Protease activity can be detected in majority of patient tumors
- CX-072 is unmasked/activated in human tumors
- CX-072 is predominantly intact in circulation

Biological Activity of CX-072

- Intratumor concentrations of unmasked/activated CX-072 are estimated to be sufficient for high-level target occupancy
- Similar concentrations are associated with efficacy in a preclinical model
- CX-072 treatment is associated with expansion of intratumoral CD8+ T cells

Conclusion

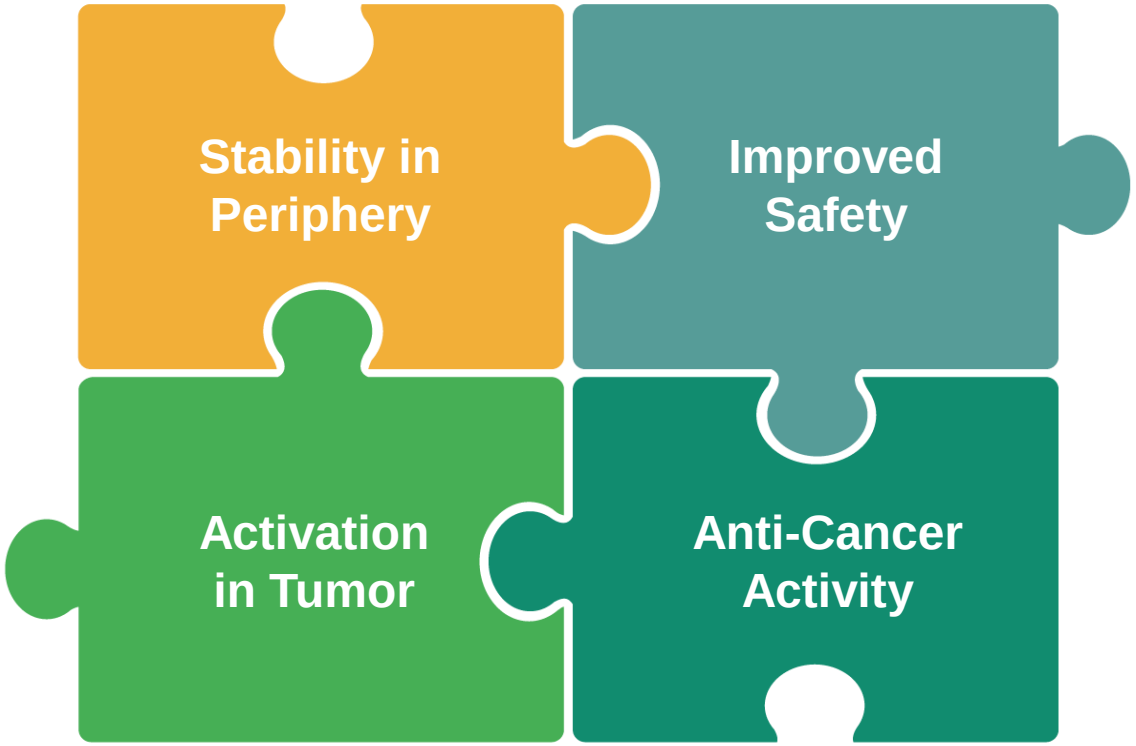
- CX-072 appears to function as designed in cancer patients
- Consistent with safety and activity of CX-072 as reported at ASCO and ESMO

CytomX Therapeutics

Summary

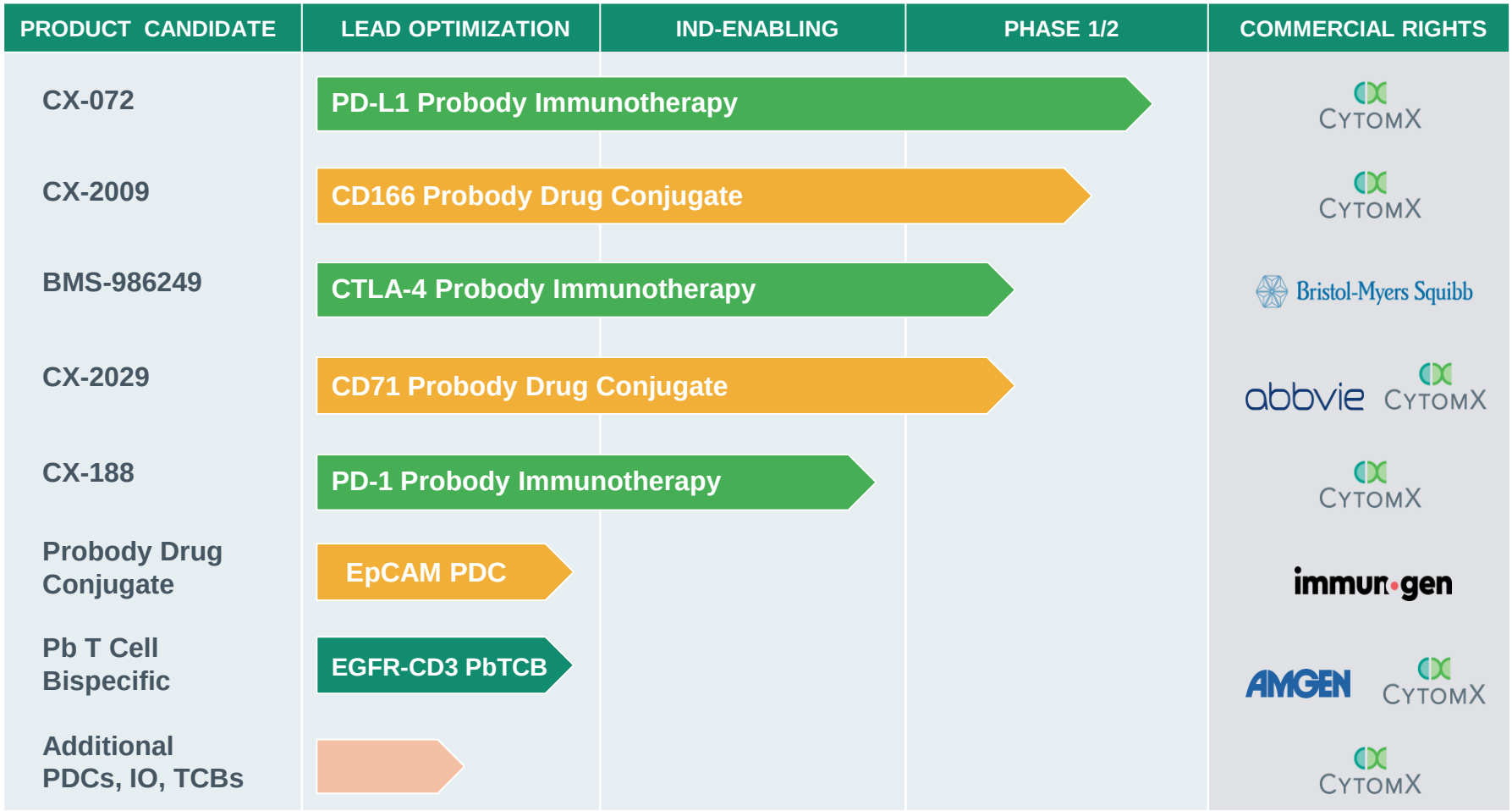
Sean McCarthy, D. Phil.
President and Chief Executive Officer

CytomX Data Presented in 2018 Provides Early Validation for Clinical Performance of the Probody Platform



- Integrated data support platform proof of concept
- Effective translation of preclinical data into clinical setting
- New paradigm for therapeutic antibodies

Deep and Differentiated Probody Pipeline



$464.6 M in cash as of end of Q318

PROCLAIM-CX-2009: CD166-Directed PDC:
Exploratory Studies in 2018-2019 Drive Potential Expansion Studies in 2019-2020

EXPLORATORY → **EXPANSION**

A: DOSE ESCALATION

Initiation: Q2 2017
Inclusion: 7 cancer types
Data Presentation: 2019

(Starting dose of 0.25 mg/kg. As of 11/2/18, dosing at 10 mg/kg)*

A2: BIOPSY REQUIRED

Initiation: Q2 2018
Inclusion: CD166+++
Data Presentation: 2019

(Starting dose of 4 mg/kg. As of 11/2/18, dosing at 9 mg/kg) *

B: COHORT EXPANSION(S)

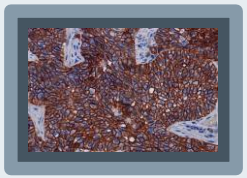
Initiation: 2018/2019
Inclusion: One or more of 7 cancer types
Data Presentation: TBA

Enrollment ongoing Trial not initiated

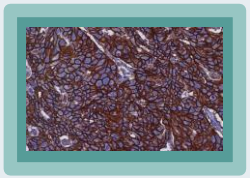
Seven CD166+ tumor types in monotherapy dose escalation arm:

- Breast cancer
- Castration-resistant prostate cancer
- Cholangiocarcinoma
- Endometrial cancer
- Head and neck cancer
- Non-small cell lung cancer
- Ovarian cancer

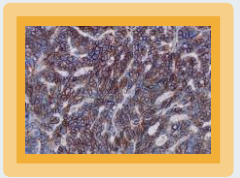
Lung cancer



Breast cancer



Ovarian cancer



Clinical Update Expected 1H 2019

CytomX Therapeutics

* CytomX Press Release November 6, 2018

2018 Achievements: Strong Execution Across Portfolio

2018 Highlights

PROCLAIM-CX-072 (PD-L1 Probody Tx)

- ✓ Presented first in human CX-072 monotherapy clinical data at ASCO and ESMO
- ✓ Presented first in human CX-072 combination clinical data with ipilimumab at ASCO and ESMO
- ✓ Presented first clinical translation data at SITC
- ✓ First platform and clinical POC for an antibody prodrug

PROCLAIM-CX-2009 (CD166 PDC)

- ✓ Monotherapy dose escalation at 10mg/kg

PROCLAIM CX-2029 (CD71 PDC)

- ✓ Phase 1/2 Trial Underway

PROCLAIM CX-188 (PD-1 Probody Tx)

- ✓ IND Filed

Upcoming Milestones

2019 Upcoming Anticipated Milestones

PROCLAIM-CX-072 (PD-L1 Probody Tx)

- Updates 2019: Monotherapy Expansions, Zelboraf® Combination

PROCLAIM-CX-2009 (CD166 PDC)

- Update 1H'19: Monotherapy Dose Escalation; PK/PD

BMS-986249 (CTLA-4 Probody Tx)

- BMS Anticipates Data Disclosures in 2019

CX-2029 (CD71 PDC)

- Trial in Progress

CX-188 (PD-1 Probody Tx)

- Trial Initiation

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Question and Answer